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Oats and bowel disease: a systematic literature review.

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Oats and bowel disease: a systematic literature review

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Abstract

Whole-grain foods such as oats may protect against colorectal cancer and have benefits on inflammatory bowel disease and coeliac disease. The present study aimed to systematically review the literature describing intervention studies that investigated the effects of oats or oat bran on risk factors for bowel disease. A literature search was conducted using Embase, Medline and the Cochrane library, which identified 654 potential articles. Thirty-eight articles describing twenty-nine studies met the inclusion criteria. Two studies carried out in participants with a history of colorectal adenomas found no effects of increased oat-bran intake on indirect risk makers for colorectal cancer. One of two interventions with oat bran in patients with ulcerative colitis showed small improvements in the patients' conditions. Most of the eleven studies carried out in adults with coeliac disease showed no negative effects of uncontaminated oat consumption. The fourteen studies carried out in volunteers with no history of bowel disease suggest that oats or oat bran can significantly increase stool weight and decrease constipation, but there is a lack of evidence to support a specific effect of oats on bowel function compared with other cereals. A long-term dietary intake of oats or oat bran could benefit inflammatory bowel disorders, but this remains to be proven. A protective effect on colorectal adenoma and cancer incidence has not yet been convincingly shown. The majority of patients with coeliac disease could consume up to 100 g/d of uncontaminated oats, which would increase the acceptability of, and adherence to, a gluten-free diet.

Key words: Oats: Bowel disease: Inflammatory bowel disease: Coeliac disease: Bowel cancer

Bowel disease represents a wide spectrum of pathologies affecting the small intestine, colon and rectum. It includes not only minor conditions such as irritable bowel syndrome (IBS) but also colorectal cancers and various types of inflammatory disorders. The latter are represented by some autoimmune disorders without clearly defined causes such as Crohn's disease (CD) and ulcerative colitis (UC) or others specifically triggered by food components such as coeliac and non-coeliac disease.

IBS produces often similar symptoms to those of inflammatory bowel disease (IBD), which includes CD and UC, but as they are not the same condition they involve very different treatments. IBS is a functional gastrointestinal disorder (and does not cause inflammation), which results in chronic abdominal pain or discomfort and diarrhoea, constipation or alternating bouts of the two. However, people with UC or

CD are also more likely to have other functional disorders such as fibromyalgia, chronic fatigue syndrome, chronic pelvic pain and temporomandibular joint disorder. Furthermore, UC and CD cause destructive chronic inflammation to the intestines that could lead to permanent damage of the intestines and harmful complications, and might require surgery and/or pharmacological treatment with steroids or immunosuppressives.

UC affects only the colon while CD can affect any part of the digestive tract. In addition to the clinical evaluation for their diagnosis using imaging and endoscopic procedures, the measurement of biomarkers such as Perinuclear Anti-Neutrophil Cytoplasmic Antibodies for UC and Anti-Saccharomyces Cerevisiae Antibody for CD, along with C-reactive protein, calprotectin and lactoferrin, can help differentiate between both inflammatory disorders. However, these tests

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; RCT, randomised controlled trials; UC, ulcerative colitis.

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are not conclusive. In some cases, patients have none of those antibodies, or both, and further tests for other antibodies (anti-OmpC, anti-CBir1, etc.) can be performed to help differentiate between those disorders.

Bowel cancer, for which environmental factors such as diet play a critical role⁽¹⁾, is the third most common cancer worldwide after lung and breast⁽²⁾. A recent systematic review on prospective observational studies evaluating the associations between dietary fibre, whole grains and risk of colorectal cancer indicates that a high intake of dietary fibre, in particular, cereal fibre and whole grains, is associated with a reduced risk of colorectal cancer: relative risk 0.90 (95% CI 0.83, 0.97) for each 10 g/d intake of cereal fibre, and relative risk 0.83 (95% CI 0.78, 0.89) for an increment of three servings daily of whole grains⁽³⁾. Whole grains are a major source of several vitamins, minerals and phytochemicals that have anticancer properties and could possibly influence the risk of colorectal cancer by various potential mechanisms⁽⁴⁾. However, the chemical composition of whole-grain foods varies greatly and could differentially influence the activity and composition of the gut microbiota (DJ Rose, in this supplement), and their potential protective effects against cancer and other chronic diseases. Therefore, it is possible that particular whole-grain foods such as oats affect various health outcomes, particularly with regard to bowel-related disorders.

This is also relevant for inflammatory bowel disorders. Europe has the highest annual incidence of IBD, with 24.3 cases per 100 000 person-years and 12.7 cases per 100 000 person-years for UC and CD, respectively⁽⁵⁾. The link between diet and IBD is not clear, but butyrate, a SCFA produced from the colonic fermentation of dietary fibres, has been shown to be effective in the reduction of UC⁽⁶⁾ and CD⁽⁷⁾, which suggests potential benefits for dietary interventions aiming to increase the production of butyrate and/or other SCFA from the gut microflora.

Coeliac disease is common, occurring in about 1% of the population worldwide^(8,9). It is traditionally characterised by chronic inflammation of the proximal small intestine that can

develop in genetically susceptible people exposed to gluten. The symptoms associated with coeliac disease can affect any area of the body, and differ greatly between individuals, but usually include headaches, diarrhoea, stomach pains and lethargy, associated with sudden or unexpected weight loss and unexplained Fe-deficiency anaemia, or other unspecified anaemia. Some patients can also develop dermatitis herpetiformis, which is a chronic blistering skin condition. Coeliac disease is diagnosed by blood test (for the presence of endomysial antibodies and tissue transglutaminase antibodies) and biopsy of the small intestine. The disease induces morphological changes of the small intestine lining showing atrophy of the villi with crypt hyperplasia, and lymphocyte infiltration, leading to nutrient malabsorption.

The treatment of coeliac disease requires life-long adherence to a gluten-free diet. Oats, compared with wheat, barley and rye, contain low levels of prolamins, the components of gluten responsible for the toxicity in susceptible individuals, and could therefore represent a good source of fibre in a gluten-free diet. Importantly, several coeliac disease organisations support, and clinical studies suggest, that oats may be consumed by adults and children with coeliac disease without adverse events^(10–13).

The purpose of the present study was to systematically review the literature describing intervention studies that had investigated the effect of long-term consumption of whole-grain oat-based products (including oat bran) on risk factors for bowel disease. The objectives of the study were (1) to summarise the large body of literature on the subject, (2) to describe the relative strengths and weaknesses of the studies and (3) to evaluate the need for large intervention trials.

Methods

Literature search

Embase, Medline and the Cochrane library (Cochrane Central Register of Controlled Trials) were searched for articles describing intervention studies with oat-based products

Table 1. Embase Classic + Embase search strategy (1947 to 26 November 2012)

No.	Search	Results
1	(oat or oats or oatcake\$ or flapjack\$ or oatmeal or porridge or muesli or granola).mp.*	9793
2	(intervention\$ or trial\$).mp.	1 897 864
3	intervention study/or early intervention/	21 882
4	'randomized controlled trial (topic)'/or controlled clinical trial/or 'phase 2 clinical trial (topic)'/or 'clinical trial (topic)'/or 'phase 1 clinical trial (topic)'/or 'controlled clinical trial (topic)'/or 'phase 3 clinical trial (topic)'/	439 432
5	2 or 3 or 4	1 897 864
6	1 and 5	1013
7	limit 6 to (human and english language and yr = '1965 – Current')	695
8	limit 7 to (embryo <first trimester > or infant <to one year > or child <unspecified age > or preschool child <1 to 6 years > or school child <7 to 12 years > or adolescent <13 to 17 years >)	87
9	7 not 8	608
10	limit 9 to (editorial or 'review')	79
11	9 not 10	529
12	limit 11 to (meta analysis or 'systematic review')	8
13	11 not 12	521

* mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword.

published before 26 November 2012. The search was limited to full-text English language articles carried out in human subjects aged 18 years or over, and excluded editorials, reviews and meta-analyses. Table 1 shows the search terms used, limits applied and number of articles identified in Embase. Similar searches were carried out in Medline and the Cochrane library databases. Additional articles were identified by searching for 'oat(s)' in the title of references in relevant articles obtained from the database search.

Study selection

The three databases identified a combined total of 1174 articles, of which 520 were duplicates (Fig. 1). Titles and abstracts of the remaining 654 articles were reviewed independently by two reviewers to identify articles describing studies that assessed the effect of oat consumption on the risk of bowel diseases. Articles were excluded if the studies were conducted in children or animals, if the intervention involved a cereal that was not oats, if the study was investigating (non-) oat cell carcinoma or if the article used OAT as an abbreviation, e.g. for oral anticoagulant therapy, occluded artery trial, oligoasthenoterato-zoospermia or organic anion

transporter. The two reviewers agreed that the full text should be obtained for 244 articles.

Of these 244 articles, a further thirty-two articles were excluded because the full text was not in English, the article did not describe an intervention study, the intervention did not involve oats or OAT was used as an abbreviation. We excluded conference abstracts, articles describing studies in which the intervention was less than 7 d (2- or 3-d interventions (*n* 3) and test meals (*n* 25)), and articles in which the effect of oats alone could not be determined or the outcomes were not relevant. Articles describing the effect of oat-bran concentrate (*n* 8), oat extracts with β -glucans (*n* 16), oat fibre from oat husks/hulls (*n* 7), oat gum (*n* 2), avenanthramide-enriched mixtures (*n* 1) and fermented oat products (*n* 1) were excluded. The exclusion of each article was agreed by two reviewers.

Data extraction

Data were extracted by one reviewer into pre-prepared tables and a 10% random sample of the data extraction was checked and agreed by a second reviewer. The data extracted included the country of study, participant characteristics (number, sex,

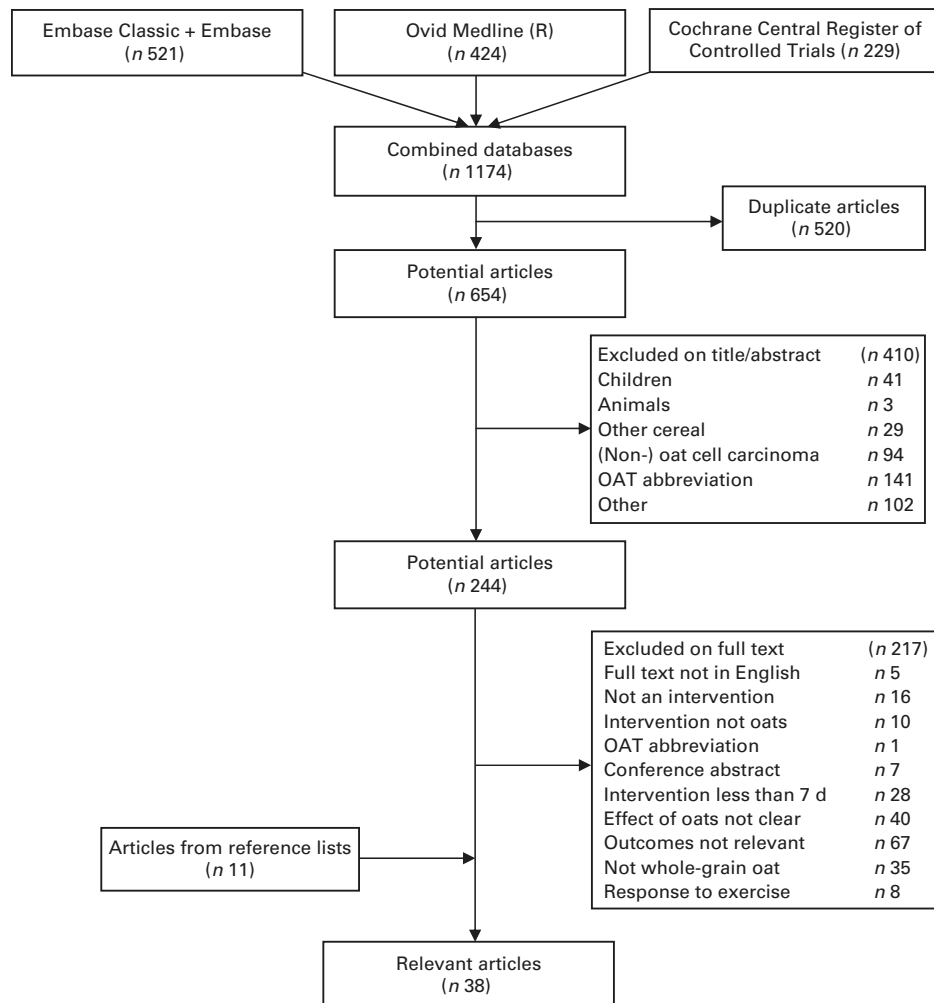


Fig. 1. Flow diagram of article selection.



age and health status), intervention characteristics (length, design and diet), variables adjusted for in the analysis and relevant outcomes. The primary outcomes of interest included characteristics of coeliac disease and UC; risk markers for colorectal cancer; stool weight, transit time and frequency; and faecal SCFA.

Quality of reporting

The Jadad scale for reporting randomised controlled trials (RCT)⁽¹⁴⁾ was used with a slight modification to score the quality of reporting of each article. Each article received one point (1) if randomisation of participants to treatment was mentioned, (2) if the method of randomisation was appropriate, (3) if blinding of the researchers/lab technicians to the intervention was mentioned, (4) if the method of blinding was appropriate and (5) if the number of all patients who started and completed the trial was clear, with reasons stated if no data were given. One point was also deducted if either the method of randomisation or blinding was considered inappropriate. Possible scores could range from 0 to 5. Studies were categorised as having a low or high quality of reporting if the total score was between 0 and 2, or 3 and 5, respectively. We also recorded the presence or absence of a sample size or power calculation for each article.

Reporting preferences

Studies were classified as RCT (1) if subjects were randomised to treatments groups, (2) if there was an appropriate control group and (3) if responses were compared between the oat and control groups. For studies that showed a statistically significant ($P < 0.05$) effect of oats consumption, the percentage change from baseline in the oat intervention group relative to the control group was the preferred outcome of interest to present. If this was not available in the article, it was calculated from the results given, and such values are indicated in the tables.

Results

We identified thirty-eight articles^(13,15–51) describing twenty-nine studies that assessed the effect of oat consumption on bowel disease (Fig. 1). Two studies were each carried out in participants with a history of colorectal adenomas^(15,16) (Table 2) or UC^(17,18) (Table 3), eleven studies (described in seventeen articles^(13,19–34)) were carried out in participants with coeliac disease (Table 4), and fourteen studies^(35–48) were carried out in participants without a history of colorectal adenomas, UC or coeliac disease (Table 5).

Colorectal cancer risk

Two studies^(15,16) were carried out in participants with a history of colorectal adenomas (Table 2). A 2-week oat-bran intervention had no significant effect on putative risk measures for colorectal cancer (colonic mucosal labelling index, mucosal labelling pattern and micronuclei per crypt)

Table 2. Characteristics of studies in participants with a history of colorectal adenomas

Study	Country	n	Participants			Health	RCT	Intervention		
			Sex	F (%)	Age (years)			Design	Length	Diet(s)
Kashan <i>et al.</i> ⁽¹⁵⁾	Canada	43 (oats) 46 (wheat)	M and F M and F	31 50	28–79 29–74	Healthy Post-polypectomy or normal colon	Yes	Parallel	2 weeks	Oat-bran or wheat-bran supplementation at 6.8 g fibre/4814 kJ (1000 kcal) (maximum of 16.4 g/d fibre)
Macrae <i>et al.</i> ⁽¹⁶⁾	Australia	20	M and F	45	36–75	With ≥ 1 adenoma removed at recent colonoscopy	Yes	Crossover	6 weeks	25 g unprocessed wheat bran or 64 g unprocessed oat bran or 38 g processed wheat bran (all bran)

F, female; RCT, randomised controlled trials; M, male.



Table 3. Characteristics of studies in participants with ulcerative colitis

Study	Participants					Intervention				
	Country	n	Sex	F (%)	Age (years)	Health	RCT	Design	Length	Diet(s)
Hallert <i>et al.</i> ⁽¹⁷⁾	Sweden	22 (oats) 10 (control)	M and F M and F	45 30	20–77 21–64	Ulcerative colitis	No	Parallel	12 weeks	60 g/d oat bran to daily diet v. no oat bran (control)
Zhang <i>et al.</i> ⁽¹⁸⁾	Sweden	9	M and F	22	27–67	Proctocolectomised for ulcerative colitis With ileostomies Good general health With ileostomies Good general health	Yes	Crossover	3 weeks	272 g/d wheat flour bread (187 g/d wheat flour) or 408 g/d oat-bran bread (135 g/d oat bran)

F, female; RCT, randomised controlled trials; M, male.

in post-polypectomy and non-polyp Canadian patients⁽¹⁵⁾. Similarly, 64 g/d of oat-bran for 6 weeks had no significant effect on measures of rectal epithelial cell proliferation (number of crypts, number of labelled cells/crypt column, number of cells/crypt column, total labelling index and percentage of labelled cells within compartments) in twenty Australian patients with recent adenomas⁽¹⁶⁾. Both articles were categorised as having a low quality of reporting.

Ulcerative colitis

Two Swedish studies^(17,18) assessed the effect of oat-bran consumption in participants with UC (Table 3). Hallert *et al.*⁽¹⁷⁾ found no signs or symptoms of colitis relapse in twenty-two patients adding 60 g/d of oat bran to their daily diet for 12 weeks. In fact, those who reported any gastrointestinal complaint at entry had a significant reduction in abdominal pain and reflux by 24 and 55 %, respectively, after consuming oat bran⁽¹⁷⁾. Zhang *et al.*⁽¹⁸⁾ found that the addition of oat-bran bread to the diet for 3 weeks in nine participants proctocolectomised for UC significantly increased the wet and dry weights of ileostomy effluent by 73 and 88 %, respectively, in comparison with wheat flour bread. The quality of reporting for both articles was considered low.

Coeliac disease

Table 4 shows the characteristics of the eleven studies carried out in patients with coeliac disease (described in seventeen articles^(13,19–34)). Three studies were carried out in the UK^(19,20,26), five in Finland^(13,21–23,25,27–30), and one each in Norway⁽²⁴⁾, Ireland^(31,32) and Sweden^(33,34). The number of subjects in each intervention group ranged from four to thirty-five, and the interventions involved consuming between 34 and 100 g/d of oats for between 14 d to 5 years. The quality of reporting for the seventeen articles^(13,19–34) was considered low (modified Jadad score between 0 and 2) for ten articles^(13,19–25,31,34) and high (modified Jadad score between 3 and 5) for seven articles^(26–30,32,33).

Analyses of intestinal biopsy specimens have mostly shown either no change or a slight improvement in various measures including ratios of surface to volume⁽²⁰⁾ and villous height to crypt depth^(25,26,30), enterocyte height^(26,31,32), villous atrophy^(13,21,23,27), villous architecture^(26,33), histomorphometric index^(13,27), morphological damage^(31,32), mononuclear-cell infiltration^(13,27), Marsh score⁽²⁴⁾, mucosal inflammation^(21,23), grade of inflammation⁽³³⁾, mucosal human leucocyte antigen DR (HLA-DR) expression^(25,29,32), enterocyte lactase expression⁽³²⁾, CD25 positive cells/1 mm²⁽³²⁾, intercellular adhesion molecule 1 (ICAM-1) (CD54) staining⁽³²⁾ and lamina propria blood vessel size⁽³²⁾. In the Norwegian study⁽²⁴⁾ however, one patient was found to be intolerant to oats and developed mucosal changes and dermatitis.

Intraepithelial lymphocyte counts were also reported to have remained within normal limits⁽²⁶⁾, or not changed significantly in five studies^(25,28,29,31,32). While a Finnish study⁽³⁰⁾ found a slight but significant increase in CD3⁺ and $\gamma\delta$ intraepithelial lymphocyte densities, the authors stated that the



Table 4. Characteristics of studies in participants with coeliac disease

Study	Participants				Intervention			
	Country	n	Sex	F (%)	Age (years)	Health	RCT	Design
Low quality of reporting (modified Jadad score 0–2)	UK	12	M and F	33	5–59	Coeliac disease	No	SC
	UK	4	–*	–	–	Coeliac disease	No	SC
	Finland	31	M and F	58	16–64	Coeliac disease	No	Cross-over
	Norway	19	M and F	89	Adults	Coeliac disease	No	SC
High quality of reporting (modified Jadad score 3–5)	Finland	11 (oats)	M and F	55	36–61	Coeliac disease	No	Parallel
	UK	10	M and F	30	30–67	DH	No	SC
	Finland	26 IR (oats)	M and F	65	48 (12)†	Coeliac disease	Yes	Parallel
	Finland	26 IR (control)	M and F	65	42 (10)	Coeliac disease	Yes	Parallel
Janatuinen <i>et al.</i> ^(27,28)	Finland	19 ND (oats)	M and F	63	42 (14)	Coeliac disease	Yes	Parallel
	Finland	21 ND (control)	M and F	76	48 (11)	Coeliac disease	Yes	Parallel
	Finland	35 (oats)	M and F	63	53 (12)	Coeliac disease	Yes	Parallel
	Finland	28 (control)	M and F	64	52 (10)	Follow-up study ^(27,28)	Yes	Parallel
Peraaho <i>et al.</i> ⁽³⁰⁾	Finland	23 (oats)	M and F	74	25–69	Coeliac disease	Yes	Parallel
	Ireland	16 (no oats)	M and F	75	22–65	Coeliac disease	No	SC
	Ireland	10	–	–	Adults	Coeliac disease	No	SC
	Sweden	15	M and F	60	22–71	Coeliac disease	No	SC

F, female; RCT, randomised controlled trials; M, male; SC, self-controlled; DH, dermatitis herpetiformis; IR, in remission; ND, newly diagnosed.

* Not available.

† Means and standard deviations (shown in parentheses).



Table 5. Characteristics of studies in participants without a history of colorectal adenomas, ulcerative colitis or coeliac disease

Study	Participants					Intervention		
	Country	n	Sex	F (%)	Age (years)	Health	RCT	Diet(s)
Low quality of reporting (modified Jadad score 0–2)								
Abrahamsson <i>et al.</i> ⁽³⁵⁾	Sweden	12 (oats) 12 (wheat)	Women		20–46	Healthy	Yes	376 g/d bread buns containing oat bran or wheat bran (20 g fibre)
Anderson <i>et al.</i> ⁽³⁶⁾	USA	10	Men		34–66	HC	No	100 g/d oat bran after control diet
Hosig <i>et al.</i> ⁽³⁷⁾	USA	9 (oats) 9 (wheat)	Men		19–28	Healthy	No	100 g/d oat bran or 30 g/d wheat bran
Judd & Truswell ⁽³⁸⁾	UK	10	M and F	40	24–37		No	125 g/d rolled oats after control diet
Kirby <i>et al.</i> ⁽³⁹⁾	USA	8	Men		35–62	88% HC	No	100 g/d oat bran or no oat bran
Kretsch <i>et al.</i> ⁽⁴⁰⁾ and Calloway & Kretsch ⁽⁴¹⁾	USA	6 (83% Caucasian 17% African American)	Men		23–40	Healthy	No	Egg formula (control) alone or with toasted or untoasted oat bran (0.6 g/kg body weight)
Kristensen & Bugel ⁽⁴²⁾	Denmark	24	M and F		22–30	Healthy	No	102 g oat bran/10 MJ or no oat bran
Marlett <i>et al.</i> ⁽⁴³⁾	USA	9	Men		23.8 (2.2)*	Healthy, NC	No	100 g/d oat bran or low-fibre diet
Noakes <i>et al.</i> ⁽⁴⁴⁾	Australia	23	M and F	43	44–64	Hypertriglyceridaemic	Yes	121/87 g/d (M/F) oat bran or low-any/lose starch diet
Sturtzel & Elmadfa ⁽⁴⁵⁾ , Sturtzel <i>et al.</i> ^(46,47)	Austria	15 (oats) 15 (control)			57–98	Multiple chronic diseases Laxative use	No	7–8 g/d oat bran or habitual diet (control)
Valle-Jones ⁽⁴⁸⁾	UK	50	M and F	64	60–80	Constipation	No	Two oat-bran biscuits per d (Lejifibre)
High quality of reporting (modified Jadad score 3–5)								
Arffmann <i>et al.</i> ⁽⁴⁹⁾	Denmark	6	Men		22–26	Healthy	Yes	18 g/d oat bran or 18 g/d breadcrumbs
Kestin <i>et al.</i> ⁽⁵⁰⁾	Australia	24	Men		29–61	HC	Yes	95 g/d oat bran, 35 g/d wheat bran or 60 g/d rice-bran
Payler <i>et al.</i> ⁽⁵¹⁾	UK	10 Caucasian	M and F	80	31–64	Slow intestinal transit	Yes	20 g/d oatmeal or wheat bran for 1 week then 40 g/d for 2 weeks

F, female; RCT, randomised controlled trials; M, male; HC, hypercholesterolaemic; SC, self-controlled; NC, normocholesterolaemic.
*Mean and standard deviation (shown in parentheses).



density was relatively mild when compared with patients treated for coeliac disease in general.

Evidence from nine studies suggests that oats consumption has little impact on serum levels of antibodies to gliadin^(13,24–26,28,31–33), reticulin^(13,26,28) or endomysium^(13,21–26,30–33) following the consumption of oats.

The addition of oats to a gluten-free diet appears to have no negative effects on nutritional status, as indicated by little change in BMI^(13,22,27,33,34), weight⁽²²⁾ or blood concentrations of vitamin A, D or E⁽²²⁾; folate or vitamin B₁₂^(20,27,30,33,34); Hb, ferritin or Fe^(27,30,33,34); Ca^(22,27); Mg⁽²²⁾; albumin^(27,33,34) or alkaline phosphatase^(33,34). However, Kempainen *et al.*⁽²²⁾ found a significant reduction in serum vitamin B₁₂ after the consumption of kilned or unkilned oats.

One study⁽²²⁾ found no significant change in serum total- or HDL-cholesterol concentrations in response to the consumption of kilned or unkilned oats. However, after 6 months of consuming a diet with unkilned oats, serum TAG concentrations decreased significantly by 24% but returned to near-baseline level after a further 6 months using kilned oats.

There were two studies^(25,26) of patients with dermatitis herpetiformis. In a UK study⁽²⁶⁾, dermal IgA showed no significant changes following oat consumption and there were no reports of pruritis or rash. In a Finnish study⁽²⁵⁾, IgA fluorescence on the skin increased in one patient only, two patients developed a transient rash and one patient withdrew due to the appearance of a persistent but mild rash, in comparison with three of the control patients who developed a transient rash and had IgA deposits on the skin. Both studies concluded that patients with dermatitis herpetiformis can include moderate amounts of oats in the diet and that the rash in these patients is not activated by eating oats.

In patients with coeliac disease, the effect of oats on gastrointestinal symptoms was varied. Symptoms included diarrhoea and flatulence^(19,24,30,33,34), nausea⁽¹⁹⁾, bloating or abdominal distension^(22,24), constipation⁽³⁰⁾ and anorexia and irritability⁽¹⁹⁾. In some studies, patients remained symptom free, had no adverse effects or there was no significant difference in symptoms compared with the control group^(20,21,26,28,31,32). Some studies showed improvements in symptoms, including a reduction in indigestion⁽³⁰⁾, improved bowel function⁽³⁴⁾ and an increase in the percentage of patients without symptoms from 50% at baseline to 67% at 24 months⁽³³⁾.

Reasons for withdrawal of patients with coeliac disease from studies included gastrointestinal symptoms such as distension and flatulence^(13,28,30,33,34) or pain^(24,30), vomiting⁽²³⁾, rash⁽¹³⁾ and worsening of itching without signs of dermatitis (in patients with dermatitis herpetiformis)^(27,28). In one study⁽¹³⁾, the main reason given for withdrawing was uncertainty of the safety of oats.

Other studies in participants without coeliac disease reported increased flatulence⁽³⁵⁾ or no significant side effects^(17,39,48) associated with oats consumption.

Bowel function

Table 5 describes the fourteen studies (seventeen articles^(35–51)) that were carried out in participants without a

history of colorectal adenomas, UC or coeliac disease. Five studies were carried out in the USA^(36,37,39–41,43), three in the UK^(38,48,51), two in Denmark^(42,49), two in Australia^(44,50) and one each in Austria^(45–47) and Sweden⁽³⁵⁾. The number of subjects in each intervention group ranged from six to fifty (with only one study containing more than twenty-four subjects per group) and the interventions lasted between at least 10 d and 12 weeks. The quality of reporting for the seventeen articles was considered low for fourteen articles^(35–48), and high for three articles^(49–51).

Oat consumption significantly increased wet and dry stool weight in six out of nine studies (from 15 to 88% increase) and five out of six studies (from 15 to 101% increase), respectively (Table 6). Stool frequency did not change significantly in five studies, improved in two studies and reduced in one study relative to wheat-bran and rice-bran interventions. Transit time decreased significantly by 17% in only one⁽³⁹⁾ out of four studies (Table 6). In addition, an American study⁽⁴⁰⁾ found no effect of toasted or untoasted oat bran on retention time of a dye marker (the period until it was no longer detectable).

Two studies in older participants with constipation have both found beneficial effects of oat bran. A UK study⁽⁴⁸⁾ found that consumption of two oat-bran biscuits per d in individuals aged 60–80 years improved bowel frequency (Table 6), increased the proportion of participants with normal stool consistency (16–84%) and reduced the proportion who had pain on defecation (20–6%). In addition, an Austrian study^(45–47) of frail nursing home residents found that adding 7–8 g/d of oat bran to the diet significantly reduced laxative use by 59% in comparison with a non-significant increase of 8% in the control group. However, a study⁽³⁵⁾ in younger women reported no significant effect of oat bran on stool consistency.

Faecal SCFA

There is a lack of evidence to support an effect of oats on faecal SCFA excretion^(15,17,44). Kashtan *et al.*⁽¹⁵⁾ found no change in faecal SCFA or butyric acid after a 2-week oat-bran RCT in participants with a history of colorectal adenomas. Similarly, Hallert *et al.*⁽¹⁷⁾ found no significant change in the faecal excretion of a variety of SCFA or in the sum of SCFA after their 12-week oat-bran intervention in participants with UC, although butyric acid was increased significantly by 36% at the fourth week and hepatonic acid was increased significantly by 100% at the eighth week. While Noakes *et al.*⁽⁴⁴⁾'s RCT found no change in the faecal excretion of acetate or propionate, the excretion of butyrate was significantly lower after 4 weeks of oat bran compared with a high-amylose diet.

Statistical analysis

Only one⁽⁴²⁾ of the thirty-eight^(13,15–51) articles described adjusting for any variables (body weight, sex, baseline values and period) in their analyses. Only two articles described carrying out a sample size or power calculation.



Table 6. Effect of oat consumption on stool weight, frequency and transit time

Comparison	Wet weight	Dry weight	Frequency	Transit time	Reference
Low quality of reporting (modified Jadad score 0–2)					
Oat bran v. wheat bran (20 g/d fibre)	—*	—	NS	—	Abrahamsson <i>et al.</i> ⁽³⁵⁾
100 g/d oat bran v. control diet	43% ↑	56% ↑	—	—	Anderson <i>et al.</i> ⁽³⁶⁾
100 g/d oat bran v. 30 g/d wheat bran	NS	NS	NS	NS	Hosig <i>et al.</i> ⁽³⁷⁾
125 g/d rolled oats v. control diet	NS	15% ↑	NS	17%† ↓	Judd & Truswell ⁽³⁸⁾
100 g/d oat bran v. no oat bran	15%† ↑	22%† ↑	—	—	Kirby <i>et al.</i> ⁽³⁹⁾
Toasted oat bran v. control	65%† ↑	92%† ↑	NS	NS	Kretsch <i>et al.</i> ⁽⁴⁰⁾ and Calloway & Kretsch ⁽⁴¹⁾
Untoasted oat bran v. control	88%† ↑	101%† ↑	NS	NS	Kristensen & Bugel ⁽⁴²⁾
102 g oat bran/10 MJ v. no oat bran	45% ↑	70% ↑	—	—	Marlett <i>et al.</i> ⁽⁴³⁾
100 g/d oat bran v. low-fibre diet	44%† ↑	—	13% ↑	—	Noakes <i>et al.</i> ⁽⁴⁴⁾
121/87 g/d (M/F) oat bran v. low-amylose starch diet	NS	—	NS	—	Sturtzel <i>et al.</i> ⁽⁴⁶⁾
7–8 g/d oat bran v. habitual diet (control)	—	—	No stool: 12 v. 64%†	—	Valle-Jones ⁽⁴⁸⁾
Two oat bran biscuits per d v. baseline	—	—	—	—	—
High quality of reporting (modified Jadad score 3–5)					
18 g/d oat bran v. 18 g/d breadcrumbs	34%† ↑	—	—	—	Affmann <i>et al.</i> ⁽⁴⁹⁾
95 g/d oat bran v. 35 g/d wheat bran	—	—	9%† ↓	—	Kestin <i>et al.</i> ⁽⁵⁰⁾
95 g/d oat bran v. 60 g/d rice bran	—	—	12%† ↓	—	—
40 g/d oatmeal v. 40 g/d wheat bran or baseline	—	—	—	NS	Payler <i>et al.</i> ⁽⁵¹⁾

M, male; f, female.

* Not reported.

† Percentage change calculated from information in original article.

Quality of reporting

For the thirty-eight articles^(13,15–51) reviewed, the total modified Jadad score ranged from 0 (13% of articles) to 4 (3% of articles). The most common total score was 1 (32%), followed by 2 (29%) and 3 (24%). Nineteen articles (50%) mentioned randomisation of participants to an intervention group, and the method of randomisation was reported and judged to be appropriate for one article. Blinding of researchers to treatment was mentioned in ten articles (26%), and the method of blinding was reported and judged to be appropriate in seven of these. The number of participants who started and completed the trial was clearly described, with the reason being stated if no data, for twenty-eight articles (74%).

Discussion

Strength and limitations of review

To our knowledge, the present study is the first systematic review to assess the effects of long-term interventions with oat products on a range of bowel functions/diseases/risk markers. Of the thirty-eight articles^(13,15–51) included in the present review, eleven were identified from the reference lists rather than from the database searches, highlighting the importance of using multiple sources to identify relevant articles. It is possible that the database search strategy missed these studies because the journals were not covered by the databases, or the terms used to identify intervention studies alone were too restrictive. It is likely that publication bias had an impact on the findings of the present review: articles showing significant results are more likely to be submitted, published or published more quickly than studies without such characteristics, and articles published in languages other than English were excluded.

The present review is limited by the small number of studies in participants with a history of colorectal adenomas or UC, and the lack of studies identified in patients with CD. The majority of studies had a small sample size and many studies lacked an appropriate control group. The studies were relatively heterogeneous in terms of the intervention diet (amount and type of oat product), the control diet used and the clinical markers reported for each condition. However, it is difficult to pinpoint specific markers for each disorder, considering the variability and complexity of symptoms and biomarkers associated with bowel disease. Therefore, future studies are required to assess the effect of different types of oat products and their dose–response effect for various bowel conditions, and such studies need to be adequately powered, contain an appropriate control group and target primary outcome measures that can be compared across studies.

Colorectal cancer

The hypothesis linking fibre intake with colorectal cancer risk was originally proposed by Burkitt⁽⁵²⁾ nearly 40 years ago. Increased stool bulk and dilution of carcinogens in the colonic lumen, reduced transit time and bacterial fermentation of fibre to SCFA have been suggested as possible mechanisms of



action⁽⁵³⁾. Recent evidence highlighted the protective role of whole-grain foods against colorectal cancer^(3,54). However, despite the observational epidemiological evidence, few intervention studies have been conducted in order to confirm the association between whole-grain consumption and decreased risk of colorectal cancer, as well as to assess the effects of specific whole-grain foods. As described in the present review, only two intervention studies with oats have been carried out in participants with a history of colorectal adenomas, and neither showed any significant effects on putative and indirect risk factors for colorectal cancer. Furthermore, these studies included only a small number of patients and had a short follow-up. It is therefore impossible to draw any conclusion with regard to the results obtained, and further research including comprehensive and well-designed trials is warranted.

Inflammatory bowel disease

Our literature search identified only two long-term intervention studies with oats in patients with UC and none in patients with CD. However, only one of these studies was relevant in terms of improvement in the patients' conditions, with a reduction in relapse and decrease in abdominal pain and reflux⁽¹⁷⁾.

Experiments with animal models suggested that a loss of tolerance to gut microbiota could be central to the pathogenesis of IBD⁽⁵⁵⁾; however, this has not been confirmed in patients with IBD. Antibiotic therapy has no beneficial effect on UC while it provides some clinical benefits in luminal CD⁽⁵⁶⁾. Defects in innate or humoral and adaptive immune response to host microbiota occur in CD^(57,58) and UC^(59,60), respectively. Drug therapy for IBD includes the use of various anti-inflammatory drugs such as aminosalicylates (PPAR γ agonist) or corticosteroids. However, probiotic therapy seems effective in inducing and maintaining remission in UC patients^(61,62), which underlines the potential benefit of using the prebiotic properties of oats as an adjuvant to probiotic/pharmaceutical treatment for UC patients.

Coeliac disease

Coeliac disease presents a wide spectrum of clinical manifestations, characterised by diarrhoea, abdominal distension and failure to thrive in young children⁽⁶³⁾, while older children and adolescents more often present atypical gastrointestinal complaints including pain, vomiting, or constipation as well as other symptoms such as arthritis, neurological symptoms, anaemia or asymptomatic silent disease⁽⁶⁴⁾. In adults, the main feature of the disease is diarrhoea⁽⁶⁵⁾, but anaemia⁽⁶⁶⁾ and osteoporosis⁽⁶⁷⁾ are also prominent. Other manifestations include villous atrophy, dermatitis herpetiformis, IBS, bloating, and chronic fatigue as well as various neurological presentations⁽⁶⁸⁾.

The results of the present review are in agreement with Thompson's review⁽⁶⁹⁾ of articles published between 1995 and 2003, and Haboubi *et al.*⁽⁷⁰⁾'s systematic review of articles published up to 2005, which show that including oats in the

diet of patients with coeliac disease has mostly no detrimental effects on the intestinal mucosa morphology and inflammation. Serum concentration of antibodies against gliadin also remained unchanged after oat consumption. Furthermore, symptoms generated by dermatitis herpetiformis were not worsened after oat consumption. The results of the present study suggest that the majority of patients with coeliac disease can tolerate up to 100 g/d of uncontaminated oats. Relieving the restrictions on oats for patients with coeliac disease could increase the acceptability of, and adherence to, a gluten-free diet.

However, it is often difficult to avoid the contamination of oats by traces of other gluten-containing cereals such as wheat cereals. Commercial oats may be processed in facilities that also process gluten-containing cereals. Contamination can also happen in the field, or during the transport of the grains, so conventionally grown, and therefore the level of contamination in processed oats can vary. It is therefore probably not appropriate to suggest that oats can be safely consumed by coeliac patients who are very sensitive to gluten. Some coeliac disease patients may also be intolerant to oats^(24,71), and there is currently no accurate estimate of the prevalence of oats intolerance in coeliac disease.

Bowel function

Dysfunctional bowel function is a common feature of many intestinal disorders such as IBS and includes abdominal pain relieved after defecation, changes in stool frequency/consistency as well as flatulence and bloating⁽⁷²⁾. Only a limited number of studies examined the effects of oats on markers of bowel function. The majority of the studies described in the present review showed no significant effect of oats on stool frequency or transit time. However, oats or oat bran significantly increased stool weight (dry and wet) and decreased constipation, which would suggest that increasing oat consumption could benefit people suffering from IBS. However, these effects do not seem to be specific to oats when comparisons with wheat or rice bran are considered^(37,50,51).

Gut motility may be one of the mechanisms linking dietary factors and physical activity with colorectal cancer risk⁽⁵²⁾. However, results of epidemiological studies are inconclusive^(73–76), and appropriately powered, well-designed RCT are required to properly assess the effects of oats on bowel function. Considering bowel function as a marker for colorectal cancer risk is currently inadequate considering the discrepancy of results obtained from epidemiological studies.

SCFA

SCFA, such as butyrate, are the product of bacterial fermentation of dietary fibre in the colon. Many studies using cell culture and animal models have assessed the effects of butyrate on colon cancer, with conflicting results⁽⁷⁷⁾. Butyrate has been shown to modulate cellular proliferation⁽⁷⁸⁾, apoptosis^(79,80) and cell differentiation⁽⁸¹⁾. The few studies that examined the effects of oat consumption on SCFA production do not support a positive effect on SCFA. All studies used



faecal SCFA concentration as a surrogate marker for SCFA production. However, such measurement does not represent the actual epithelial exposure. Inter- and intra-individual SCFA productions are also highly variable due to many confounders such as recent dietary intake, colonic transit and hydration status. Therefore, the interpretation of such data is greatly limited.

Conclusion

Long-term dietary intake of oats or oat bran could present some benefits for patients with IBS and UC. A protective effect on colorectal adenoma and cancer is plausible but it has not been convincingly shown. Relieving the restrictions on oats for patients with coeliac disease could increase the acceptability of, and adherence to, a gluten-free diet. However, further research including comprehensive and well-designed trials is required to assess the efficacy of increased oat consumption against bowel disorders.

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